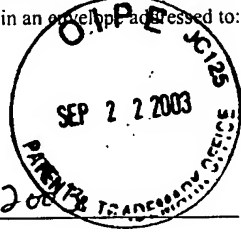


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PATENT  
Attorney Docket No.: 016930-005000US



On September 15, 2003

TOWNSEND and TOWNSEND and CREW LLP

By: Mark T. Davis

**IN THE UNITED STATES PATENT AND TRADEMARK OFFICE**

In re application of:

GREGORY et al.

Application No.: 10/602,258

Filed: June 23, 2003

For: ADENOVIRAL VECTORS  
HAVING A PROTEIN IX DELETION

Examiner: Not Yet Assigned

Art Unit: Not Yet Assigned

INFORMATION DISCLOSURE  
STATEMENT UNDER 37 CFR §1.97 and  
§1.98

Commissioner for Patents  
P.O. Box 1450  
Alexandria, VA 22313-1450

Sir:

The references cited on attached form PTO/SB/08B are being called to the attention of the Examiner. In accordance with 37 CFR §1.98(d), copies of the references can be found in Application No. 08/328,673, filed October 25, 1994, now U.S. Patent 6,210,939 B1 issued April 3, 2001 (Attorney Docket No. 016930-000920US ). It is respectfully requested that the cited references be expressly considered during the prosecution of this application, and the references be made of record therein and appear among the "references cited" on any patent to issue therefrom.

As provided for by 37 CFR 1.97(g) and (h), no inference should be made that the information and references cited are prior art merely because they are in this statement and no

representation is being made that a search has been conducted or that this statement encompasses all the possible relevant information.

Applicant believes that no fee is required for submission of this statement.

However, if a fee is required, the Commissioner is authorized to deduct such fee from the undersigned's Deposit Account No. 20-1430. Please deduct any additional fees from, or credit any overpayment to, the above-noted Deposit Account.

Respectfully submitted,



Chuan Gao  
Reg. No. 54,111

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First Named Inventor	Gregory, Richard
Art Unit	Not Yet Assigned
Examiner Name	Not Yet Assigned
Attorney Docket Number	016930-005000US

**U.S. PATENT DOCUMENTS+**

Examiner Initials*	Cite No. <sup>1</sup>	Document Number Number Kind Code <sup>2</sup> (if known)	Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear
	AA	US-6,210,939 B1	04-03-2001	Gregory et al.	

**FOREIGN PATENT DOCUMENTS**

Examiner Initials*	Cite No. <sup>1</sup>	Foreign Patent Document			Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear	T <sup>2</sup>
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	AB	WO	94/24297		10/1994			<input type="checkbox"/>

**NON PATENT LITERATURE DOCUMENTS**

Examiner Initials *	Cite No. <sup>1</sup>	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.	T <sup>2</sup>
	AC	Aiello et al. Adenovirus 5 DNA Sequences Present and RNA Sequences Transcribed in Transformed Human Embryo Kidney Cells (HEK-Ad-5 or 293) Virology 94:460-469 (1979).	
	AD	Aulitzky et al. "Recombinant Tumour Necrosis Factor Alpha Administered Subcutaneously or Intramuscularly for Treatment of Advanced Malignant Disease: a Phase I Trial." Eur. J. Cancer 27(4) :462-467 (1991).	
	AE	Austin, E.A. and Huber, B.E. "A First Step in the Development of Gene Therapy for Colorectal Carcinoma: Cloning, Sequencing, and Expression of Escherichia coli Cytosine Deaminase." Eur. J. Cancer 27(4) :462-467 (1991).	
	AF	Bacchetti, S. and Graham, F. "Inhibition of cell proliferation by an adenovirus vector expressing the human wild type p53 protein." International Journal of Oncology 3:781-788 (1993).	
	AG	Baker et al. "Suppression of Human Colorectal Carcinoma Cell Growth by Wild-Type p53." 249:912-915 (1990).	
	AH	Bartek et al. "Aberrant expression of the p53 oncoprotein is a common feature of a wide spectrum of human malignancies." Oncogene 6:1699-1703 (1991).	
	AI	Berkner, Kathleen L. and Sharp, Phillip A. "Effect of the tripartite leader on synthesis of a non-viral protein in an adenovirus 5 recombinant." Nucleic Acids Research 13(3) :841-857 (1985).	
	AJ	Boshart et al. "A Very Strong Enhancer Is Located Upstream of an Immediate Early Gene of Human Cytomegalovirus." Cell 41:521-530 (1985).	
	AK	Bressac et al. "Abnormal structure and expression of p53 gene in human hepatocellular carcinoma." Proc. Natl. Acad. Sci. (USA) 87:1973-1977 (1990).	
	AL	Caruso et al. "Regression of established macroscopic liver metastases after in situ transduction of a suicide gene." Proc. Natl. Acad. Sci. (USA) 90:7024-7028 (1993).	

Examiner  
SignatureDate  
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	AM	Smith, R.R. et al., "Studies of the use of viruses in the treatment of carcinoma of the cervix," Cancer 9(6) :1211-1218 (1956).						
	AN	Wills, K.N. et al., "Adenovirus vectors for gene therapy of cancer," Genetically Targeted Research & Therapeutics: Antisense & Gene Therapy Abstract S216, Apr. 12-18, 1993.						
	AO	Zhang, W.W. et al., "High-efficiency gene transfer and high-level expression of wild-type p53 in human lung cancer cells mediated by recombinant adenovirus," Canc. Gene Ther. 1(1) :5-13 (1994).						
	AP	Challberg, M.D. and Kelly, T.J. PNAS USA, 76:655-659 (1979).						
	AQ	Chen et al. "Genetic Mechanisms of Tumor Suppression by the Human p53 Gene." Science 250:1576-1580 (1990).						
	AR	Chen et al. "Expression of wild-type p53 in human A673 cells suppresses tumorigenicity but not growth rate." Oncogene 6:1799-1805 (1991).						
	AS	Cheng et al. "Suppression of Acute Lymphoblastic Leukemia by the Human Wild-Type p53 Gene." Cancer Research 52:222-226 (1992).						
	AT	Colby, W.W. and Shenk, T.J., "Adenovirus Type 5 Virions Can be Assembled in Vivo in the Absence of Detectable Polypeptide IX" Virology 39:977-980 (1981).						
	AU	Culver et al. "In Vivo Gene Transfer with Retroviral Vector-Producer Cells for Treatment of Experimental Brain Tumors" Science 256:1550-1552 (1992).						
	AV	Culver et al. "Lymphocytes as a cellular vehicles for gene therapy in mouse and man." Proc. Natl. Acad. Sci. USA 88:3155-3159 (1991).						
	AW	Demetri et al. "A Phase I Trial of Recombinant Human Tumor Necrosis Factor and Interferon-Gamma: Effects of Combination Cytokine Administration In Vivo." J. Clin. Oncol. 7(10) :1545-1553.						
	AX	Diller et al. "p53 Functions as a Cell Cycle Control Protein in Osteosarcomas." Mol. Cell. Biology 10:5772-5781 (1990).						
	AY	El-Deiry et al. "WAF1, a Potential Mediator of p53 Tumor Suppression." Cell 75:817-825 (1993).						
	AZ	Ezzidine et al. "Selective Killing of Glioma Cells in Culture and in Vivo by Retrovirus Transfer of the Herpes Simplex Virus Thymidine Kinase Gene." The New Biologist 3:608-614 (1991).						
	BA	Feinstein et al. "Expression of the normal p53 gene induces differentiation of K562 cells." Oncogene 7:1853-1857 (1992).						
	BB	Freeman et al. "The "Bystander Effect": Tumor Regression When a Fraction of the Tumor Mass Is Genetically Modified." Cancer Res. 53:5274-5283 (1993).						

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	BC		Ghosh-Choudhury et al. "Protein IX, a minor component of the human adenovirus capsid, is essential for the packaging of full length genomes." EMBO Journal 6:1733-1739 (1987).			
	BD		Gooding et al. "Molecular Mechanisms by Which Adenoviruses Counteract Antiviral Immune Defenses." Crit. Rev. Immunol. 10:53-71 (1990).			
	BE		Graham, F.L. and van der Eb, A.J. "A New Technique for the Assay of Infectivity of Human Adenovirus 5 DNA." Virology 52:456-467 (1973).			
	BF		Graham, F.L. and Prevec, L. Vaccines: New Approaches to Immunological Problems. R. W. Ellis (ed.), Boston: Butterworth-Heinemann, 363-390 (1992).			
	BG		Heuvel et al. "Association between the cellular p53 and the adenovirus 5 E1B-55kd proteins reduces the oncogenicity of Ad-transformed cells." EMBO Journal 9:2621-2629 (1990).			
	BH		Hock et al. "Mechanisms of rejection induced by tumor cell-targeted gene transfer of interleukin 2, interleukin 4, interleukin 7, tumor necrosis factor, or interferon .gamma.. " Proc. Natl. Acad. Sci. USA 90:2774-2778 (1992).			
	BI		Hollstein et al. "p53 Mutations in Human Cancers." Science 253:49-53 (1991).			
	BJ		Horwitz, Marshall S. "Adenoviridae and Their Replication." sVirology B.N. Fields (ed.), New York: Raven Press, 1679-1721 (1990).			
	BK		Horvath, J. and Weber, J.M. "Nonpermissivity of Human Peripheral Blood Lymphocytes to Adenovirus Type 2 Infection." J. Virol. 62:341-345 (1988).			
	BL		Huang et al. "A cellular protein that competes with SV40 T antigen for binding to the retinoblastoma gene product." Nature 350:160-162 (1991).			
	BM		Huber et al. "Retroviral-mediated gene therapy for the treatment of hepatocellular carcinoma: An innovative approach for cancer therapy." Proc. Natl. Acad. Sci. USA 88:8039-8043 (1991).			
	BN		Hunter, T. "Braking the Cycle." Cell 75:839-841 (1993).			
	BO		Jones, N. and Shenk, T. "Isolation of Adenovirus Type 5 Host Range Deletion Mutants Defective for Transformation of Rat Embryo Cells." Cell 17:683-689 (1979).			
	BP		Kamb et al. "A Cell Cycle Regulator Potentially Involved in Genesis of Many Tumor Types." Science 264:436-440 (1994).			
	BQ		Kuerbitz et al. "Wild-type p53 is a cell cycle checkpoint determinant following irradiation." Proc. Natl. Acad. Sci. USA 89:7491-7495 (1992).			

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	BR		Landmann et al. "Prolonged Interferon-.gamma. Application by Subcutaneous Infusion in Cancer Patients: Differential Response of Serum CD14, Neopterin, and Monocyte HLA Class I and II Antigens." J. Interferon Res. 12(2) :103-111 (1992).				
	BS		Lane, D.P. "p53, guardian of the genome." Nature 358:15-16 (1992).				
	BT		Lee et al. "Human Retinoblastoma Susceptibility Gene: Cloning, Identification, and Sequence." Science 235:1394-1399 (1987).				
	BU		Lemaistre et al. "Therapeutic effects of genetically engineered toxin (DAB.sub.486 IL-2) in patient with chronic lymphocytic leukaemia." Lancet 337:1124-1125 (1991).				
	BV		Lemarchand, Patricia. "Adenovirus-mediated transfer of a recombinant human .alpha..sub.1 -antitrypsin cDNA to human endothelial cells." Proc. Natl. Acad. Sci. USA 89:6482-6486 (1992).				
	BW		Levine, A.J. "The Tumor Suppressor Genes." Annu. Rev. Biochem. 62:623-651 (1993).				
	BX		Lowe et al. "p53 is required for radiation-induced apoptosis in mouse thymocytes." Nature 362:847-852 (1993).				
	BY		Lowe et al. "p53-Dependent Apoptosis Modulates the Cytotoxicity of Anticancer Agents." Cell 74:957-967 (1993).				
	BZ		Mercer, et al. "Negative growth regulation in a glioblastoma tumor cell line that conditionally expresses human wild-type p53." Proc. Natl. Acad. Sci. USA 87:6166-6170 (1990).				
	CA		Metzger, Gerard and Werbin, Harold. "Evidence for N-Acetoxy-N-2-acetylaminofluorene Induced Covalent-like Binding of Some Nonhistone Proteins to DNA in Chromatin." Biochemistry 18(4) :655-659 (1979).				
	CB		Moolten, F.C. "Tumor Chemosensitivity Conferred by Inserted Herpes Thymidine Kinase Genes: Paradigm for a Prospective Cancer Control Strategy." Cancer Res. 46:5276-5281 (1986).				
	CC		Nakabayashi et al. "Transcriptional Regulation of .alpha.-Fetoprotein Expression by Dexamethasone in Human Hepatoma Cells." The Journal of Biological Chemistry 264:266-271 (1989).				
	CD		Palmer et al. "Genetically modified skin fibroblasts persist long after transplantation but gradually inactivate introduced genes." Proc. Natl. Acad. Sci. USA 88:1330-1334 (1991).				
	CE		Rao et al. "The adenovirus E1A proteins induce apoptosis, which is inhibited by the E1B 19-kDa and Bcl-2 proteins." Proc. Natl. Acad. Sci. USA 89:7742-7746 (1992).				
	CF		Ravoet et al. "Non-Surgical Treatment of Hepatocarcinoma." Journal of Surgical Oncology Supplement 3:104-111 (1993).				
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	CG		Rich et al. "Development and Analysis of Recombinant Adenoviruses for Gene Therapy of cystic Fibrosis." Human Gene Therapy 4:461-476 (1993).			
	CH		Rosenfeld et al. "In Vivo Transfer of the Human Cystic Fibrosis Transmembrane Conductance Regulator Gene to the Airway Epithelium." Cell 68:143-155 (1992).			
	CI		Sarnow et al. "Adenovirus E1b-58kd Tumor Antigen and SV40 Large Tumor Antigen Are Physically Associated with the Same 54 kd Cellular Protein in Transformed Cells." Cell 28:387-394 (1982).			
	CJ		Shaw et al. "Induction of apoptosis by wild-type p53 in a human colon tumor-derived cell line." Proc. Natl. Acad. Sci. USA 89:4495-4499 (1992).			
	CK		Siegfried, W. "Perspectives in Gene Therapy with Recombinant Adenoviruses." Exp. Clin. Endocrinol. 101:7-11 (1993).			
	CL		Sorscher et al. "Tumor cell bystander killing in colonic carcinoma utilizing the Escherichia coli DeoD gene to generate toxic purines." Gene Therapy 1:233-238.			
	CM		Spector, David J. "The Pattern of Integration of Viral DNA Sequences in the Adenovirus 5-Transformed Human Cell Line 293." Virology 130:533-538 (1983).			
	CN		Stewart et al. "Difference imaging of adenovirus: bridging the resolution gap between X-ray crystallography and electron microscopy." EMBO Journal 12:2589-2599 (1993).			
	CO		Supersaxo et al. Pharm. Res. 5(8) :472-476 (1988).			
	CP		Straus, S.E. "Adenovirus infections in humans." The Adenoviruses. H.S. Ginsberg (ed.), New York: Plenum Press, 451-496 (1984).			
	CQ		Takahashi et al. "p53: A Frequent Target for Genetic Abnormalities in Lung Cancer." Science 246:491-494 (1989).			
	CR		Takahashi et al. "Wild-type but not Mutant p53 Suppresses the Growth of Human Lung Cancer Cells Bearing Multiple Genetic Lesions." Cancer Research 52:2340-2343 (1992).			
	CS		Thimmappaya et al. "Adenovirus VAI RNA Is Required for Efficient Translation of Viral mRNAs at Late Times after Infection." Cell 31:543-551 (1982).			
	CT		Wang et al. "Quantitation of mRNA by the polymerase chain reaction." Proc. Natl. Acad. Sci. USA 86:9717-9721 (1989).			
	CU		Watanabe et al. "Cell-specific Enhancer Activity in a Far Upstream Region of the Human .alpha.-Fetoprotein Gene." The Journal of Biological Chemistry 262:4812-4818 (1987).			

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	CV	White et al. "The 19-Kilodalton Adenovirus E1B Transforming Protein Inhibits Programmed Cell Death and Prevents Cytolysis by Tumor Necrosis Factor .alpha.." Mol. Cell. Biol. 12:2570-2580 (1992).					
	CW	Wills et al. Human Gene Therapy 5:1079-1088 (1994).					
	CX	Yonish-Rouach et al. "Wild-type p53 induces apoptosis of myeloid leukaemic cells that is inhibited by interleukin-6." Nature 352:345-347 (1991).					
	CY	Casez et al., Oncogene, vol. 6(10), pp. 1791-1797, 1991.					
	CZ	Haj-Ahmad and Graham, Development of a helper-independent human adenovirus vector and its use in the transfer of the herpes simplex virus thymidine kinase gene, J. Virol. 57(1): 267-274, Jan. 1986.					
	DA	Winnacker, E.L., From Genes to Clones, pp. 342-343, VCH Publishers, New York, NY, 1987.					

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